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EXAMINER

HAMA, JOANNE

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 07/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No. 10/088,139	Applicant(s) ECKERT ET AL.	
	Examiner Joanne Hama, Ph.D.	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 December 2002.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 December 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This Application, filed December 17, 2002, is a 371 of PCT/FR00/02623, filed September 22, 2000 and claims priority to foreign application 99/12,017, filed September 27, 1999 in France.

Applicants have filed an amendment to the claims March 15, 2002. Claims 3, 6, 7, and 8 have been amended. Claims 1-8 are pending.

### ***Information Disclosure Statement***

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Pages 29-32 of the specification contain a listing of references. If these references are to be considered by the Examiner, they must be listed on an IDS and copies of each reference must be submitted.

Applicants have listed a letter from Dalie on the IDS. While this letter has been considered by the Examiner, it has been crossed off the IDS list because it is not a publication.

### ***Claim Rejections - 35 USC § 101***

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35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-5 encompass transgenic human. This is non-statutory matter. Rewriting the claims to read, "non-human animal" would overcome this rejection.

Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The applicant claims transgenic animals wherein the transgenic animal expresses a multmutated form of presenilin 1 (PS1) and wherein the transgenic animal exhibits an apoptotic phenotype in its renewable peripheral tissue. The claimed animals are not supported by a specific, substantially asserted, or well-established utility. The specification discloses that the transgenic mice of the instant invention are comprised of a transgene construct comprising a nucleic acid sequence encoding a presenilin 1 protein comprising 5 amino acid substitutions operably linked to a human HMG-CoA reductase promoter. The specification teaches that these transgenic mice exhibit higher levels of spontaneous apoptosis in its T lymphocytes (e.g. see specification, Figure 2 and 3). While the specification teaches these embodiments of the claimed mice, nothing in the specification or the art teaches that there is a relationship between PS1, T lymphocytes, apoptosis, and Alzheimer's disease. In other words, the claimed animals would be used in a study to further determine the relationship between PS1, T lymphocytes, apoptosis, and Alzheimer's disease. Further,

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while the specification points out the relationship between PS1 and Alzheimer's disease (AD), wherein AD is characterized by intracellular neurofibrillary deposits and extracellular deposits of the  $\beta$ -amyloid (A $\beta$ ) peptide forming the amyloid plaques (specification, page 1, 2<sup>nd</sup> parag.) in the brain, the claimed invention encompasses a relationship between PS1 and apoptosis in T lymphocytes. This characteristic is not supported or well established by the art or the specification. In addition to this, nothing in the art or specification teach a relationship between apoptotic T cells and Alzheimer's disease. Further, nothing in the art or specification teaches a relationship between apoptotic T cells and any neurodegenerative disease. Thus, the transgenic cells and animals of the instant invention have no specifically identified utility, rather, the specific utility of the transgenic cells and mammals of the instant invention requires further research to identify or reasonably confirm. (see *Brenner, Comr. Pats. v. Manson*, 148 USPQ 689 (US SupCt 1966).

Applicant is referred to the Revised Utility Examination Guidelines published December 21, 1999 in the Federal Register, Volume 64, Number 244, pages 71441-71442 for the required specific and substantial utility. "A claimed invention must have a specific and substantial utility. This requirement excludes 'throw-away' 'unsubstantial' or 'non-specific' utilities," (column 3, 3rd paragraph of page 71441). In the current Office practice, utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A claim to a transgenic animal whose use is disclosed as an "experimental model" would not be considered to be specific in the absence of guidance from the art or the

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specification as to what the relationship is between PS1, T lymphocytes, and apoptosis. As noted above, since the specification fails to teach the relationship between PS1 and apoptosis in T lymphocytes associated with Alzheimer's disease, the specification fails to meet the requirements for demonstrating a specific, substantial, or well-established utility for the instant invention as claimed.

Claims 1-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some

experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claimed invention encompasses any multimutated form of presenilin 1 (PS1), wherein apoptosis is detected in any renewable peripheral tissue. The specification teaches that transgenic mice comprising a human PS1 comprising 5 point mutations that results in amino acid changes from a M to an L at position 146 (M146L), a H to a R at position 163 (H163R), an A to an E at position 246 (A246E), an L to a V at position 286 (L286V), and a C to a Y at position 410 (C410Y) operably linked to a human HMG-CoA reductase promoter (specification, page 21, Example 1) exhibit a higher rate of apoptosis in their T lymphocytes as compared to wild type mice (e.g. see specification, Figures 2 and 3). While the specification teaches these embodiments, nothing in the art

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or specification teaches an artisan a relationship between PS1 and apoptosis. Further, nothing in the art or specification teaches the relationship between PS1 comprising amino acid substitutions and apoptosis. Nothing in the art or specification provides guidance that certain amino acid mutations or certain combinations of amino acid mutations in PS1 are related to any biological event associated with apoptosis. Therefore, the artisan would need to establish a relationship between PS1 and apoptosis before the claimed transgenic animal or a cell obtained from the claimed animal can be used in a method for screening for compounds. As such, in view of the quantity of experimentation necessary to establish the biological relationship between PS1 and apoptosis and the lack of guidance as to what steps one would need to take to establish the relationship, it would have required undue experimentation to use the claimed invention.

The claimed invention encompasses any transgenic animal expressing a multimutated form of any presenilin 1. While the specification teaches transgenic mice comprising a human PS1 comprising 5 point mutations that results in amino acid changes from a M to an L at position 146 (M146L), a H to a R at position 163 (H163R), an A to an E at position 246 (A246E), an L to a V at position 286 (L286V), and a C to a Y at position 410 (C410Y) operably linked to a human HMG-CoA reductase promoter (specification, page 21, Example 1), the art at the time of filing teaches that an artisan cannot predict that every transgene construct will have activity in any transgenic animal. An art example demonstrating the unpredictability in making transgenic animals using



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the same transgenic construct in different species of animal is demonstrated by Hammer et al. (1990, Cell, 6: 1099-1112). Hammer et al. created both transgenic mice and rats expressing the human HLA-b27 gene and beta-2 microglobulin. Although both transgenic animals bearing the HLA-b27 gene expressed the gene, transgenic mice did not show any HLA-b27 associated disease, whereas the transgenic rats demonstrated most of the HLA-b27 related diseases (Hammer, et al., page 1099, col. 2, lines 20-28). This result shows that the integration of a transgene into an alternative species may result in widely different phenotype responses even in animals of the same species. Additionally, promoters and enhancer elements may not function in all the species because they may require specific cellular factors. With regards to the instant invention, the specification does not provide any guidance as to whether a given promoter used for expressing an exogenous gene in one animal would have been functional in other animals and even if the promoter may have been active, whether the level of the transgenic product produced would have been sufficient to produce a certain phenotype. Therefore, it would have been undue experimentation for an artisan to practice the claimed invention for the broad scope of any transgenic animal comprising human PS1 comprising 5 point mutations that results in amino acid changes from a M to an L at position 146 (M146L), a H to a R at position 163 (H163R), an A to an E at position 246 (A246E), an L to a V at position 286 (L286V), and a C to a Y at position 410 (C410Y) operably linked to a human HMG-CoA reductase promoter. According to the teachings of Hammer, et al. an artisan cannot reasonably predict what

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characteristics any animal comprising the human presenilin expression construct would have and thus, the claimed invention is limited to a transgenic mouse.

The claimed invention encompasses any transgenic animal expressing a multmutated form of any presenilin 1. While the specification teaches transgenic mice comprising a nucleic acid sequence encoding a human PS1 comprising 5 point mutations (PS15M) that results in amino acid changes from a M to an L at position 146 (M146L), a H to a R at position 163 (H163R), an A to an E at position 246 (A246E), an L to a V at position 286 (L286V), and a C to a Y at position 410 (C410Y) operably linked to a human HMG-CoA reductase promoter (specification, page 21, Example 1), the art at the time of filing teaches that an artisan cannot necessarily predict what phenotype any transgenic animal comprising a transgene construct will have. The art at the time of filing teaches that making any transgenic animal was unpredictable. One reason for this unpredictability stems from the randomness in which the transgene integrates into the host's genome. Cameron (1997, Molecular Biotechnology, 7: 253-265) teaches, "a feature common to many transgenic experiments is the unpredictability transgenic lines produced with the same construct frequently displaying different levels of expression. Further, expression levels do not correlate with the number of transgene copies integrated. Such copy-number-independent expression patterns emphasize the influence of surrounding chromatin on the transgene (Cameron, page 256, section 4 on transgene regulation and expression)." Thus, an artisan cannot predict where a transgene will integrate in the host genome, how many copies of a transgene will integrate into the host genome, what the transgene expression pattern is, of the

resulting transgenic animal (with regards to how much transcript is produced by the cell and with regards to in which tissues express transgene, as enhancers from the host's genome may also influence transgene expression), and what the subsequent phenotype(s) is of the transgenic animal. As summarized by Mench (1999, Transgenic Animals in Agriculture, eds. Murray et al., CAB International: Oxon, pages 251-268), "because there can be so much variation in the sites of gene insertion, the numbers of gene copies transferred, and gene expression, every transgenic animal produced using microinjection is (theoretically, at least) unique in terms of its phenotype (Mench, page 259, bottom)." With regards to the instant invention, while the specification teaches the phenotype exhibited by transgenic mice comprising a nucleic acid sequence encoding PS15M operably linked to a human HMG-CoA reductase promoter, the specification does not teach that other transgenic animals comprising a nucleic acid sequence encoding human PS15M operably linked to a human HMG-CoA reductase promoter have a similar phenotype. Nothing in the specification teaches an artisan how to predict the phenotypes of all transgenic animals comprising a nucleic acid sequence encoding human PS15M operably linked to a human HMG-CoA reductase promoter. It would be undue experimentation for an artisan to predict the phenotypes for all transgenic animals comprising a nucleic acid sequence encoding human PS15M operably linked to a human HMG-CoA reductase promoter without guidance. As the specification provides guidance for transgenic mice a nucleic acid sequence encoding human PS15M operably linked to a human HMG-CoA reductase promoter, the artisan is enabled to practice the claimed invention for these transgenic mice only.

The claimed invention is to a transgenic animal comprising a multimutated form of presenilin, wherein the transgenic animal exhibits apoptosis in any renewable peripheral tissue. While the specification teaches that apoptosis was detectable in T lymphocytes (specification, page 17 describes how T lymphocytes were obtained; Examples 2-7 describe assays that were used to monitor the effects of presenilin1 and its mutant forms on T lymphocytes), and indicates that renewable peripheral tissue encompasses the spleen, liver, and blood (specification, page 6, 1<sup>st</sup> parag.), nothing in the specification teaches an artisan that apoptosis was detectable in other renewable peripheral tissue such as the spleen and liver of any transgenic animal comprising a multimutated form of presenilin. According Nilsberth et al., (1999, The Histochemical Journal, 31: 515-523), while high levels of presenilin 1 mRNA was found in testis, kidney, spleen, adrenal gland, thymus, skeletal muscle, liver, small intestine, and lung, these tissues are not affected in Alzheimer's disease (Nilsberth et al, abstract). While Nilsberth et al. teach that certain tissues express high levels of PS1, an artisan cannot predict that if certain tissues were to express mutant PS1, that those tissues will have any PS1-related pathology. Further, no indication was given what that pathology would be. While it may be that the claimed invention, wherein the invention is comprised of a transgenic animal that expresses a PS15M, does exhibit apoptosis in tissues such as spleen and liver, the specification does not teach an artisan that this is the case. Nothing in the specification teaches an artisan that apoptosis is detectable in cells obtained from the spleen and liver of these transgenic animals, nor does the specification teach that there is a common element in renewable peripheral tissue that

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expression of PS15M induces apoptosis. Further, with regards to the broad scope of lymphocytes, the specification teaches that apoptosis was detectable in T lymphocytes, but does not teach that apoptosis was in B lymphocytes. It also should be pointed out that "renewable peripheral tissue," in addition to spleen and liver, encompasses epithelial tissues such as skin and the lining of the intestine. Nothing in the specification teaches an artisan that there was an increase in apoptosis the skin or intestine of transgenic animals comprising PS15M. It would be undue experimentation for an artisan to practice the claimed invention because nothing in the specification or the art provide guidance to an artisan as to what common feature(s) is necessary between peripheral tissues such that expression of multimutated PS1 would result in apoptosis. The specification does not enable an artisan to use any renewable peripheral tissue or cell from any renewable peripheral tissue beyond this scope.

The claimed invention encompasses transgenic animals that express a mutated form of presenilin 1, wherein the mutations are amino acid substitutions comprising M146L, H163R, A246E, L286V, C410Y, I143T, L235P, P264L, P267S, E317G, G384A, L392V, A426P, and/or P436S. The claimed invention broadly encompasses a multimutated human presenilin1 comprising at least three of these mutations (specification, page 4, parag. 5). The specification teaches that transgenic mice expressing presenilin1M5 (presenilin 1 comprising the mutations M146L, H163R, A246E, L286V, C410Y; PS1M5) were made (specification, Example 1). The specification teaches that spontaneous apoptosis is greatly increased in the transgenic mice expressing the multimutated PS1M5 (specification, page 23, 1<sup>st</sup> parag.). The

specification also teaches that after culturing for 2.5 hours without apoptotic stimuli, lymphocytes from transgenic mice expressing PS1M5 demonstrated more spontaneous apoptosis than lymphocytes from PS1 and PS1M146L mice (specification, page 23, 2<sup>nd</sup> parag., Figure 3). While the specification teaches these embodiments of transgenic mice expressing PS1M5, the specification does not teach an artisan what combination of amino acid substitutions in PS1 would result in mice or animals that exhibit apoptosis in renewable peripheral tissue. It would be undue experimentation for an artisan to make the claimed invention because no guidance was provided as to what regions of PS1 are associated with any apoptotic pathway. Further, no guidance was provided as to what amino acid changes influence structure changes of PS1, such that apoptosis would occur in peripheral tissue. For this reason, the specification only enables an artisan to practice the claimed invention for transgenic mice comprising PS1M5.

The claimed invention encompasses a method for detecting compounds intended for the treatment of any neurodegenerative disease, wherein the animals in claims 1-5 are used to screen for these compounds. The claimed invention also encompasses a method for the treatment of any neurodegenerative disease, wherein a cell obtained from the animals of claims 1-5 are used to screen for these compounds. The claimed invention broadly encompasses any neurodegenerative disease. This includes diseases such as Parkinson's disease, Tay-Sachs, and Lou Gehrig's disease. While the claims encompass these embodiments, nothing in the specification teaches that the transgenic mice comprising human PS15M exhibit any of the pathology associated with any neurodegenerative diseases such as Parkinson's, Tay-Sachs, and Lou Gehrig's

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diseases. Alternatively, nothing in the specification teaches that any neurodegenerative disease, other than Parkinson's disease has a relationship with PS1. In addition to this, nothing in the specification teaches that the transgenic mouse expressing PS15M has any symptoms associated with Alzheimer's disease. As such, an artisan does not know what symptoms of Alzheimer's disease one should monitor when screening for compounds which are used to treat Alzheimer's disease in PS1M5 transgenic mice or in cells obtained from these mice. It would be undue experimentation for an artisan to practice a method of screening for compounds intended to treat any neurodegenerative disease because the specification does not provide guidance that there is any relationship between any multimutated PS1 and any neurodegenerative disease or symptoms of neurodegeneration. Therefore, the specification does not enable an artisan to use any of the transgenic animals in claims 1-5 comprising multimutated PS1 or any cell obtained from the transgenic animals of claims 1-5 as a screen for compounds to treat any neurodegenerative disease.

Therefore, for the reasons described above, the specification does not provide guidance to the artisan commensurate with the scope of the claims.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at <http://www.uspto.gov/web/menu/current.html#register>).

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The written description requirement for a claimed genus is satisfied by sufficient description of a representative number of species by actual reduction to practice and by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show applicant were in possession of the claimed genus.

While the specification and the art provides adequate written description for a mammalian sequence encoding PS1, the specification does not provide adequate description for the broad scope of any presenilin 1 obtained from non-mammalian species. In addition to this, while the art and the specification teach that a variety of amino acid substitutions in PS1 have been isolated from Alzheimer's patients, the specification does not teach how to make any multimutant PS1, such that the mutant



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PS1 has a role in increasing apoptosis in peripheral tissue, aside from human PS15M. In addition to this, the claims are broad for any multimutated form of PS1 (claim 1), such that the claims encompass any mutation, anywhere in PS1, using any amino acid substitution. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). In the instant case, while the Applicants indicate the possible mutations of PS1 that could be comprised in the instant invention (claim 4), the specification does not indicate how to select a certain combination of mutations such that an artisan can predictably make a multmutant PS1 that increases apoptotic activity in peripheral tissue. In addition to this, while claim 1 broadly encompasses any PS1 comprising multiple mutations anywhere in the PS1 protein, the specification does not teach an artisan what region(s) of PS1 one should target to make a PS1 protein that increases apoptotic activity in peripheral tissue. Further, the specification does not teach what amino acids one should use in the targeted region. The skilled artisan cannot envision all the possible variant amino acid sequences which would result in a multmutant PS1 protein with increased apoptotic activity, and therefore conception is not achieved until reduction to practice

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has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a mammalian PS1 comprising of 5 amino acid substitutions wherein M is substituted for L at position 146 of the human sequence, H is substituted for R at position 163 of the human sequence, A is substituted for E at position 246 of the human sequence, L is substituted for V at position 286 of the human sequence, and C is substituted for Y at position 410 of the human sequence meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

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regards as the invention. Claim 4 is unclear because the claim appears to be read as a PS1 comprising 13 or 14 mutations. However, claim 5, then, cannot depend on claim 4.

### ***Conclusion***

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

ANNE M. WEHBE' PH.D  
PRIMARY EXAMINER

A handwritten signature in black ink, consisting of stylized, overlapping loops and a long horizontal stroke extending to the right.